Remarks

I. Support for the Amendments

Support for the foregoing new claim amendments may be found throughout the specification, and in the original claims. No new matter was added by way of these amendments.

II. Status of the Claims

Upon entry of the foregoing amendment claims 1-27 will be pending and claims 1-3 and 13-16 will have been withdrawn from consideration. New claims 17-27 have been added, claims 4-12 have been rejected and claims 4-9, and 11-12 have been amended.

III. Summary of the Office Action

In the Office Action dated January 15, 2002, the Examiner has made objections to the specification and claims and has rejected the claims under 35 U.S.C. § 112, first paragraph, 35 U.S.C. § 112, second paragraph, 35 U.S.C. § 103(a). Applicants respectfully offer the following remarks to overcome or traverse each of the elements of the Office Action. Reconsideration and allowance are respectfully requested.

IV. Response to Objection – Sequence Compliance

In the Office Action at page 3, the Examiner asserts that the instant application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences but fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825. In response, Applicants have filed herewith a paper copy of the sequence listing and a computer readable form of the sequence listing, and have also amended the specification to refer to the sequence listing in accordance with 37 C.F.R. 1.821 through 1.825. However, it is noted that Applicants did not receive a copy of a Notice to Comply with the outstanding Office Action. As such, Applicants have not returned a copy of a Notice to Comply with this Response. Nonetheless, Applicants submit that the application complies with the sequence listing requirements, and respectfully request withdrawal of this objection.

V. Response to Objection – Oath or Declaration

The Examiner asserts that the oath or declaration filed on September 20, 2000 is defective because non-initialed and non-dated alterations have been made to the declaration. Applicants will be filing a substitute oath or declaration in compliance with 37 C.F.R. 1.67(a) shortly. Accordingly, Applicants request that the Examiner hold this objection in abeyance pending receipt of the substitute declaration.

VI. Response to Objection –Specification

The Examiner has objected to the title of the invention because, allegedly, the title is not descriptive. The Examiner asserts that a new title is required that is clearly indicative of the invention to which the claims are directed and suggests "Mutant E. coli KAS II With Altered Substrate Specificity" as a title. The Examiner is thanked for the suggestion, however Applicants respectfully traverse this objection and submit that the title of the invention is indeed indicative of the claimed invention. While the suggested title does relate to certain embodiments of the invention, the invention is broader than mutant *E. coli* KAS II proteins. As such, withdrawal of this objection is respectfully requested.

The Examiner has objected to the drawings because, allegedly, Figure 12, page 2 is not present in the specification. In response, Applicants have filed herewith a substitute Figure 12 which includes page 2. Applicants submit that corrected Figure 12 does not contain new matter. It is submitted that the corrected figure is fully supported by the specification and figures as filed, and merely corrects an obvious typographical error in the figure as originally filed which one of skill in the art would recognize the existence of, as well as recognize the appropriate correction for. *See* MPEP § 2163.07 (II).

More particularly, Figure 12 provides a multiple amino acid sequence alignment of known β-Ketoacyl-ACP synthase protein sequences. However, the figure as originally filed was missing page 2 which depicts the amino acid residues which align with amino acid residues 121-240 of the reference sequence. Nonetheless, as Figure 12 discloses known amino acid sequences of organisms unambiguously identified in the figure and specification as filed. As such, one of skill would clearly recognize that there was an obvious typographical error in original Figure 12.

Once one of skill recognizes this obvious typographical error, it would be well within their ability to obtain the known, unambiguously identified full amino acid sequences to thereby determine the appropriate correction to the figure. As such, it is respectfully submitted that the addition of missing page 2 of Figure 12 is fully supported in the present specification and original figures, and thus does not constitute new matter. Accordingly withdrawal of this objection is respectfully requested.

VII. Response to Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 4-12 have been rejected under 35 U.S.C. § 112, Second Paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner argues that the use of the term "encoding" in claims 4-7 is confusing. In response, Applicants have amended independent claim 4 to replace the term "encoding" with "of" to clarify the claims. However, such amendment does not narrow the scope of the claims in any respect. Therefore, it is submitted that this rejection is now moot and should be withdrawn.

The Examiner also alleges that claims 5-7, 9 and 11 are indefinite due to the recitation of the phrase "sequence is obtained from." The Examiner asserts that this phrase is confusing because the claimed sequences would not be directly obtained from prokaryotic, *E. coli*, or plant sources. While not agreeing that the claims were indefinite as originally drafted, in order to facilitate prosecution, Applicants have amended the claims to provide that the native β-Ketoacyl-ACP synthase protein recited in the relevant independent claim is obtained from prokaryotic, *E. coli*, or plant sources. However, again, such amendment does not narrow the scope of the original claims in any respect. As such, Applicants submit that the claims are definite, and respectfully request that this rejection be withdrawn.

Further, the Examiner asserts that claims 4-12 are unclear because, allegedly, Applicants have not provided the amino acid sequence of a reference KAS polypeptide necessary for a determination of the position of the claimed mutations. Again, while not agreeing that the claims were indefinite as originally drafted, in order to facilitate prosecution, Applicants was amended

the claims to include a reference sequence of a native β-Ketoacyl-ACP synthase protein. As such, Applicants submit that the claims are definite, and respectfully request that this rejection be withdrawn.

In sum, it is respectfully submitted that the claims comply with 35 U.S.C. § 112, second paragraph, and withdrawal of these rejections are respectfully requested.

VII. Response to Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 4-12 under 35 U.S.C. § 112, first paragraph, as claiming subject matter having an insufficient written description in the specification. Applicants respectfully traverse this rejection.

The Examiner argues that the claimed invention is directed to KAS amino acid sequences that have not been disclosed in the specification. The Examiner acknowledges that, the specification teaches *E. coli* KAS II with the mutations set forth in Figure 7, but alleges that the specification fails to teach any other KAS amino acid sequences encompassed by the claimed invention or structural features of KAS amino acid sequences.

Applicants respectfully disagree. The purpose of the written description requirement is simply to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *See, Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. Further, "a description as filed is presumed to be adequate, unless and until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption." *Federal Register* 66(4):1107, Written Description Guidelines (2001).

Contrary to the Examiner's assertion, the specification discloses the hydrophobic fatty acid/cerulenin binding pocket of the KAS protein, which is a structural feature, not limited to *E. coli* KAS II. *See specification* at page 5, lines 24-25. The specification also discloses specific amino acid residues included in the binding pocket that can be engineered to provide altered substrate specificity. *See specification* at page 5, line 28 to page 6, line 5; *see, also, specification* at page 7, lines 13-22. One skilled in the art will understand that the disclosed structures are

applicable to the amino acid sequences of Figure 12, which discloses an amino acid sequence alignment of KAS protein sequences from plant, bacterial, mammalian, and other organisms. Thus, the specification discloses several engineered β-Ketoacyl-ACP synthase protein amino acid sequences and provides a written description that would reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. Accordingly, it is respectfully submitted that this rejection is improper and should be withdrawn.

The Examiner has rejected claims 4-12 under 35 U.S.C. § 112, first paragraph because, allegedly, the specification fails to provide an enabling disclosure of any organism with any substitution. Applicants respectfully traverse this rejection.

Applicants submit that the specification discloses several amino acid sequences and discloses how they can be engineered to produce the claimed amino acid sequences. Contrary to the Examiner's assertion, the specification does not only disclose how *E.coli* KAS sequences can be modified. For example, Figure 12 discloses an amino acid sequence alignment of KAS protein sequences from plant, bacterial, mammalian, and other organisms. In addition the specification discloses how amino acid sequences can be analyzed and engineered to modify substrate specificities in general. *See* Specification at page 7, line 10 to page 8, line 13; *see, also,* Specification at page 17, line 10 to page 18, line 16. Furthermore, in Examples 1 and 2, though applied to *E.coli*, the specification teaches general principles of how an KAS II / cerulenin complex can be made and studied to identify amino acid residues near cerulenin binding pockets that can be modified to affect KAS protein specificity. *See*, *e.g.*, Specification at page. 21, line 23 to page. 22, line 40. The specification also discloses particular mutations in E. coli that result in altered substrate specificity and further teaches that the disclosed ranges of mutations can also be engineered in plant KAS proteins. *See* Specification at page 8, lines 14-28; *see, also*, page 18, line 20 to page 22, line 12. Thus, the specification teaches one skilled in the art how to engineer β-Ketoacyl-ACP synthase protein sequences from a wide variety of organisms, including those sequences and organisms disclosed in Figure 12. The scope of the claimed invention is not improperly extensive and undue in view of the specification and, accordingly, this rejection is improper and should be withdrawn.

In sum, it is respectfully submitted that the claims comply with 35 U.S.C. § 112, first paragraph, and withdrawal of these rejections are respectfully requested.

VIII. Response to Rejection Under 35 U.S.C. § 103(a)

Claims 8 and 9 have been rejected under 35 U.S.C. § 103(a) as being obvious over Huang *et al.*, EMBO J 17:1183-91 ("Huang") in view of Edwards *et al.*, FEBS Letters, 402:62-6 ("Edwards"). Applicants respectfully traverse this rejection.

The claimed invention would not have been obvious to one of ordinary skill in the art at the time of the invention because there was no motivation to combine the references. The Examiner argues that one of ordinary skill in the art at the time of the invention would have been motivated to combine the teachings of Huang and Edwards and thereby to replace the residues recited in Huang so as to analyze the effect of specific mutations in the *E. coli* KAS II polypeptide on the polypeptide's enzymatic activity. Applicants respectfully disagree and submit that the Examiner's applies an impermissible obvious to try standard. A suggested motivation for combining references is obvious to try where the suggested motivation is to "explore a new technology or general approach that seems to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *See* MPEP 2145 (citing *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)).

Edwards is directed to an expression system that provides a means for further research, *i.e.*, assessing the effect of specific mutation in KAS genes. Edwards does not teach or suggest specific gene modifications or how KAS amino acid sequences can be modified to affect enzymatic activity. Huang discloses the structure of native *E. coli* KAS II and discloses amino acid residues at various positions lining a substrate-binding pocket. Huang does not teach or suggest particular functions of the particular residues. In view of the prior art of record, the Examiner's suggested motivation to isolate residues and their roles in catalysis is merely an exploration of a general approach that seems to be a promising field of experimentation. Thus, applicants submit that no motivation to combine the cited references has been provided and the

Examiner has not established prima facie obviousness. Therefore, it is respectfully submitted that this rejection is improper and should be withdrawn.

Claims 8-10 have been rejected under 35 U.S.C. § 103(a) as being obvious over Moche *et al.*, *J. Biol Chem*, 274:6031-34 ("Moche") in view of Edwards *et al.*, *FEBS Letters*, 402:62-6 ("Edwards"). Applicants respectfully traverse this rejection.

The claimed invention would not have been obvious to one of ordinary skill in the art at the time of the invention because there was no motivation to combine the references. The Examiner argues that one of ordinary skill in the art at the time of the invention would have been motivated to combine the teachings of Moche and Edwards and thereby to replace the hydrophobic residues recited in Moche with amino acids having a hydrophilic side chain. Allegedly, one of ordinary skill would have been motivated to combine these references in order to analyze the effect of altering the hydrophobicity on the *E. coli* KAS II hydrophobic binding site.

Applicants respectfully disagree and submit that the Examiner uses an impermissible obvious to try standard for establishing motivation to combine. As discussed above, a suggested motivation for combining references is obvious to try where the suggested motivation is to "explore a new technology or general approach that seems to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *See* MPEP 2145 (citing *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)). Moche, like Edwards, does not teach or suggest specific benefits to be derived from replacing the claimed amino acid residues. The motivation of analyzing the effect of altering the hydrophobicity on the *E. coli* KAS II hydrophobic binding site is merely an exploration of a general approach that seems to be a promising field of experimentation. Thus, applicants submit that no motivation to combine the cited references has been provided and the Examiner has not established prima facie obviousness. Therefore, this rejection is obvious and should be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Should the Examiner have any questions regarding this application, the Examiner is encouraged to contact Applicants' undersigned representative at (202) 942-5000.

Respectfully submitted,

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Version with markings to show changes made

IN THE SPECIFICATION:

On page 1, Please add the following paragraph, before the paragraph entitled "TECHNICAL FIELD":

INCORPORATION OF SEQUENCE LISTING

A paper copy of the Sequence Listing and a computer readable form of the sequence listing on diskette, containing the file named SeqList.txt, which is 103 kilobytes in size (measured in MS-DOS), and which was created on April 11, 2002.

IN THE CLAIMS:

Please amend claims 4-9, and 11-12 as follows:

4. (AMENDED) An amino acid sequence [encoding] of [a β-Ketoacyl-ACP synthase] an engineered β-Ketoacyl-acyl carrier protein synthase protein wherein said amino acid sequence of said engineered β-Ketoacyl-acyl carrier protein synthase protein has at least one substitution, insertion or deletion of at least one amino acid residue of an amino acid sequence of a native β-Ketoacyl-acyl carrier protein synthase, and wherein said engineered β-Ketoacyl-acyl carrier protein synthase protein has an altered substrate specificity compared to said native β-Ketoacyl-acyl carrier protein synthase protein.

5. (AMENDED) The amino acid sequence of claim 4, wherein said [amino acid sequence] native β-Ketoacyl-acyl carrier protein synthase protein is obtained from a prokaryotic source.

6. (AMENDED) The amino acid sequence of claim 4, wherein said [amino acid sequence] native β-Ketoacyl-acyl carrier protein synthase protein is obtained from [*E. coli*] *Escherichia coli*.

7. (AMENDED) The amino acid sequence of claim 4, wherein said [amino acid sequence] native β-Ketoacyl-acyl carrier protein synthase protein is obtained from a plant source.

8. (AMENDED) An amino acid sequence [encoding a β-Ketoacyl-ACP synthase] of an engineered β-Ketoacyl-acyl carrier protein synthase protein wherein said amino acid sequence of said engineered β-Ketoacyl-acyl carrier protein synthase protein has at least one substitution, insertion or deletion of at least one amino acid residue of an amino acid sequence of a native β-Ketoacyl-acyl carrier protein synthase protein selected from the group consisting of [residue] residues 105-120, 130-140, 190-205 and 340-400 of said amino acid sequence of said native β-Ketoacyl-acyl carrier protein synthase protein.

9. (AMENDED) The amino acid sequence of claim 8, wherein said [amino acid sequence] native β-Ketoacyl-acyl carrier protein synthase protein is obtained from [*E. coli*] *Escherichia coli*.

11. (AMENDED) The amino acid sequence of claim 8, wherein said [amino acid sequence] native β-Ketoacyl-acyl carrier protein synthase protein is obtained from a plant source.

12. (AMENDED) The amino acid sequence of claim 11 wherein said at least one amino acid substitution, insertion or deletion is in a position selected from the group consisting of [residue] residues 110, 113, 115, 116, 134, 139, 198, and 204 of said native β-Ketoacyl-acyl carrier protein synthase protein.